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Assistant Commissioner for Patents
Washington, D.C. 20231

On May 17, 2004

TOWNSEND and TOWNSEND and CREW LLP

By: Sylvia Arnold


PATENT
Attorney Docket No.: 021706-000810US

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Tony Wai-Chiu So et al.

Application No.: 10/124,197

Filed: April 16, 2002

For: PHARMACEUTICAL COMPOSITION

Customer No.: 20350

Confirmation No. 1659

Examiner: Sharmila S. Gollamudi

Technology Center/Art Unit: 1616

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Albert Zorko Abram, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both, under 18 U.S.C. § 1001, and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

1. All statements herein made of my own knowledge are true and statements made on information or belief are believed to be true.

2. I am currently employed by Connetics Australia Pty Ltd, the assignee of the subject application.

3. I am a Senior Chemist –Technical IP Associate and have been in pharmaceutical research since 1987. I have been employed doing dermatological product development for the last 16 years. My *Curriculum Vitae* is of record.

4. I have reviewed and analyzed the above-referenced patent application, and I am familiar with the contents therein.

5. It is my understanding that the Examiner alleges in the Office Action dated October 17, 2003 that, in the Declaration under 37 C.F.R. § 1.132 submitted on April 1, 2003 ("the 2003 Declaration"), Applicants did not provide the identity and amount of the components in the inventive foam formulation used for the side-by-side comparison with the foam formulation of Di Schiena (U.S. Patent No. 4,866,067). For the reasons set forth herein, the Examiner's concerns are overcome.

6. As described in the 2003 Declaration, the formulation set forth in column 3, Example 3(e) of Di Schiena, entitled "Foam," was prepared in our laboratory at Connetics Australia following the teaching of Di Schiena with an understanding of the foam art.

7. Exhibit A contains a true copy of a page from a Connetics' laboratory notebook, with the date redacted therefrom. As shown in Exhibit A, the Di Schiena foam ("comparative") was prepared according to the teaching set forth in Example 3(e) of Di Schiena. An accepted hydrocarbon propellant (*i.e.*, Propellant P70) was substituted for the chlorofluorocarbon propellant of Di Schiena at an amount to produce a foam of acceptable quality (*see*, the 2003 Declaration).

8. The foam as disclosed in the subject application ("inventive") was prepared in our laboratory according to the following formulation:

| Component | % w/w |
|---|---|
| Minoxidil | 4.75 |
| Ethanol | 53.645 |
| Purified Water | 31.410 |
| Butylated Hydroxytoluene | 0.095 |
| Lactic Acid (90%) | 1.00 |
| Citric Acid | 0.10 |
| Stearyl Alcohol | 0.50 |
| Cetyl Alcohol | 1.10 |
| Polysorbate 60 | 0.40 |
| Propylene Glycol | 2.00 |
| Propellant P70 | 5.00 |
| Total | 100.00 |

9. Exhibit B contains a true copy of a page from my notebook, with the date redacted therefrom, disclosing the formulation set forth in the table above.

10. As described in the 2003 Declaration, I have performed a side-by-side comparison of the inventive foam against the comparative foam and found unexpected properties in the

inventive foam that were not present in the comparative foam, including foam consistency, stability, and advantageous mechanical shear properties.

The declarant has nothing further to say.

Albert Zorko Abram

12 May, 2004
Date

SK 715

Experiment: 187/6

Title: Minoxidil Foam I.P. evaluation

Aim:

① Prepare a sample of the "Di-Shiera" formulation
② Review last temperature stability results to date

Experimental:

The following "Di-Shiera" formulation was prepared. Ref: 5% P70 replaced the 10% 114 propellant in the patent formula.

| | | Batch | First cut 1/1 |
|---|---|---|---|
| ⓐ | Minoxidil | 92137 | 3.0 g |
| ⓑ | Nicotinic Acid-N-Oxide | 21063 | 2.0 g |
| ⓒ | Propylene glycol | 22583 | 9.0 g |
| ⓓ | Isopropyl alcohol | 21645 | 4.5 g |
| ⓔ | Cetyl alcohol | 95679 | 1.8 g |
| ⓕ | Stearic acid | 21391 | 0.9 g |
| ⓖ | Laureth-4 | 24495 | 4.7 g |
| ⓗ | Water | – | 64.1 g |
| | Propellant P70 | 25099 | 5.0 g |

Items ① to ⑤ were mixed at room temperature and formed clear solution

Items ⑥ and ⑦ were added and the mixture was warmed to 80°C but a clear solution did not form

On cooling this formed a thin lotion/gel.

When the propellant was added the thin gel/lotion gelled significantly forming a laminar surfactant structure and dissimilar to 70% SLES. Would this happen with propellant 12

I don't know

Experiment No 1

# SOLTEC RESEARCH *Innovation in Drug Delivery*

**Manufacturing Dossier**
**Strictly confidential**



Soltec Item description: 5% Minoxidil Mousse
Soltec Formula: F112/29/03
Soltec Batch Number: E126/10/01

## Batch Record

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | ***Phase 1*** | | | | | | |
| 1 | Ethanol 100AG 22 | 22004 | 10.00 | 500.00 | 500.0 | | Beaker Tare: 276.82 |
| 2 | Polysorbate 60 | 21371 | 0.40 | 20.00 | 20.0 | | + theoretical mass (g) 600.0 |
| 3 | Stearyl alcohol | 21364 | 0.50 | 25.00 | 25.0 | | 876.82. |
| 4 | Cetyl alcohol | 21365 | 1.10 | 55.00 | 55.0 | | |
| | ***Phase 2*** | | | | 600.0 | | Ethanol added to correct for evap. losses. (total mass 876.8g) |
| 5 | Ethanol 100AG22 | 22004 | 43.645 | 2182.25 | 2185.7 | | |
| 6 | Butylated hydroxytoluene | 21368 | 0.095 | 4.75 | 4.8 | | |
| 7 | Purified Water | 6-Jan-02 | 31.410 | 1570.50 | 1582.2 | | |
| 8 | Citric acid | 21369 | 0.10 | 5.00 | 5.0 | | |
| 9 | Minoxidil | 20105 | 4.75 | 237.50 | 237.8 | | Beaker tare: 1000.26 |
| 10 | Lactic Acid (90%) | 21363 | 1.00 | 50.00 | 49.9 | | + theoret. mass (g): 4165.4 |
| | Propylene Glycol | 21367 | 2.00 | 100.00 | 100.0 | | 5165.66 |
| | ***Phase 3*** | | | | 4165.4 | | |
| | Propellant P70 | 20229 | 5.00 | 250.00 | | | ethanol added to correct for evap. losses (total mass: 5.17kg) |
| | Total | | 100.00 | 5,000.00 | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Aluminium PAM lined cans 65 x 125mm | | 1 | | | |
| | Valve YL 33383 | | 1 | | | |